Thromboembolic complications following trauma

Daniel F. McLaughlin, Charles E. Wade, Howard R. Champion, Jose Salinas, and John B. Holcomb

BACKGROUND: Some studies have reported an increased incidence of thomboembolic complications following trauma.
STUDY DESIGN AND METHODS: We performed a literature review and queried the National Trauma Data Bank to more closely examine the incidence of a variety of thromboembolic complications following injury.
RESULTS: Thromboembolic events are rare, but occur at a greater rate in more severely injured patients. It is unclear, however, whether the incidence of thromboembolic complications in trauma patients is on the rise overall. Differences in study populations, particularly injury severity scores, as well as different methods of screening, diagnosis, prophylaxis, and treatment have led to extreme differences in reported rates.
CONCLUSION: While recent research has added to the body of knowledge, continued efforts focusing on risk stratification, diagnosis, screening, prophylaxis, and treatment are necessary to rationally understand the spectrum of thrombotic complications.

ABBREVIATIONS: BCVI = blunt cerebrovascular injury; DVT = deep vein thrombosis; EAST = Eastern Association for the Surgery of Trauma; ICU = intensive care unit; ISS = Injury Severity Score; LMWH = low-molecular-weight heparin; MI = myocardial infarction; NTDB = National Trauma Data Bank; PE = pulmonary embolism; VTE = venous thromboembolism.

From the U.S. Army Institute of Surgical Research, Fort Sam Houston, Texas; and the Uniformed Services University of the Health Sciences, Bethesda, Maryland.

Address reprint requests to: Charles E. Wade, PhD, United States Institute of Surgical Research, 3400 Rawley E. Chambers Avenue, Fort Sam Houston, TX 78234; e-mail: charles.wade@amedd.army.mil.

The opinions or assertions expressed herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Department of the Army or the U.S. Department of Defense.

doi: 10.1111/j.1537-2995.2008.01989.x

TRANSFUSION 2009;49:256S-263S.

INTRODUCTION

Thromboembolism has long been recognized as a complication in survivors of significant injury.[1] Deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infarction (MI), cerebrovascular accidents, and mesenteric thrombosis are examples of such complications. Several factors influence the development of thrombi. Virchow's triad of a hypercoagulable state, venous injury, and stasis are frequently all simultaneously present in the injured patient. In addition to these physiologic derangements, it is estimated that hypercoagulable disorders, such as factor V Leiden and hyperhomocysteinemia, may be present in as many as 20 percent of the general population.[2] Several unique characteristics of injured patients limit the degree to which conclusions can be extrapolated from studies focused on medical or elective surgical patients. Because of differences in the patient populations analyzed and the diagnostic modalities used to detect events, significant differences in the rates of thromboembolic complications have been reported.

There have been several recent reviews focusing on the identification, prevention, and treatment of DVT and PE in trauma patients.[3-5] There are also multiple studies investigating stroke and neurologic outcomes in blunt cerebrovascular injuries (BCVIs). In contrast, few reports of MI or mesenteric thrombosis in the postinjury period exist. Aspects such as risk factor identification, ideal modes of diagnosis, effective means of prevention, and optimal forms of treatment continue to be examined. As prohemostatic agents are being used more frequently in trauma, it is important to understand the natural history of thrombotic complications in patients who survive their initial injury. Simply attributing increased rates of thrombotic complications to usage of prohemostatic agents in uncontrolled studies of severely injured patients will only confuse rather than enlighten this area of research. No single paper has adequately reviewed the five major thrombotic events after injury; thus this review will describe the ambiguity and recent literature regarding PE and DVT and more closely examine the incidence of cerebrovascular accidents, MI, and mesenteric thrombosis in injured patients.

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE **01 DEC 2009**	2. REPORT TYPE **N/A**	3. DATES COVERED **-**
4. TITLE AND SUBTITLE **Thromboembolic complications following trauma**		5a. CONTRACT NUMBER 5b. GRANT NUMBER 5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) **McLaughlin D. F., Wade C. E., Champion H. R., Salinas J., Holcomb J. B.,**		5d. PROJECT NUMBER 5e. TASK NUMBER 5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX 78234**		8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)		10. SPONSOR/MONITOR'S ACRONYM(S) 11. SPONSOR/MONITOR'S REPORT NUMBER(S)
12. DISTRIBUTION/AVAILABILITY STATEMENT **Approved for public release, distribution unlimited**		
13. SUPPLEMENTARY NOTES		
14. ABSTRACT		
15. SUBJECT TERMS		

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT **unclassified**	b. ABSTRACT **unclassified**	c. THIS PAGE **unclassified**	**UU**	**8**	

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std Z39-18

DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

Seventy years ago, DVT and PE were acknowledged as potential risks following injury.[1] In the interval we have learned a great deal about these phenomena, but identifying high-risk patients and determining the ideal means of screening, diagnosis, prevention, and treatment are still a challenge. Several obstacles are encountered in attempting to delineate the incidence of DVT or PE following injury. Studies vary greatly in time periods covered, inclusion and exclusion criteria, severity of injury, and presence or absence of standardized protocols, thus introducing significant bias. In 2004, Knudson and colleagues[3] published a review of venous thromboembolism (VTE) after trauma. That report reflected a common concern that the incidence of VTE varies greatly depending on the specific population studied, the means of detection, and the method and compliance with prophylaxis. The incidence of DVT has been observed to be as high as 58 percent in high-risk trauma patients who received neither anticoagulants nor mechanical compression devices and who were screened with venography.[6] In contrast, the rate of VTE has been documented to be as low as 0.8 percent in injured patients receiving low-molecular-weight heparin (LMWH) and followed with surveillance color-flow duplex imaging, and still lower at 0.2 percent as reported in the American College of Surgeons National Trauma Data Bank (NTDB).[7,8] This represents a nearly 300-fold difference in reported incidence.

Since the Knudson review, there have been several reports pertaining to the incidence of VTE in trauma. Stawicki and colleagues[9] presented a 10-year experience from the Pennsylvania Trauma Outcome Study in which trauma patients were stratified as high-risk if they had sustained one or more of the following injuries: pelvic fracture, lower extremity fracture, severe closed head injury (Abbreviated Injury Scale score $\geq$3) or spinal cord injury. More than 73,000 patients were identified as high-risk based upon the presence of the factors mentioned earlier. Although the number of non-high-risk patients evaluated was not noted, the incidence of DVT in the high-risk group was 1.9 percent while that in the non-high-risk group was 0.6 percent. This trend held true for PE as well, with 0.5 percent of the high-risk trauma patients experiencing PE with a 0.2 percent incidence in the lower-risk group. Both of the differences were statistically significant ($p = 0.001$). In the high-risk group, the incidence of DVT ranged from 1.3 percent in patients with fractures solely of the lower extremity to 5.4 percent in patients with both pelvic and lower extremity fractures as well as closed head injuries. PE also increased from 0.4 to 1.2 percent in the above populations. In a logistic regression model, only increasing Injury Severity Score (ISS) was found to predict the likelihood of developing DVT or PE. Possible explanations given for the low observed rates of DVT and PE were reporting bias, a truly low rate of the complications, or limited screening, although no specific mention of screening methods was made in this study. This article postulates that prior reports with higher incidences of VTE may have focused on smaller samples of patients at the highest risk, therefore leading to exaggerated rates. However, without standardization of the means of screening or event detection, it is difficult to compare these results with other studies. There is also no mention of whether pharmacologic prophylaxis or mechanical compression devices were used in these patients. It is unlikely that this population, which includes a 10-year period of injured patients at all levels of care, represents a standardized system of screening, prophylaxis, and diagnosis, all of which greatly influence the reported rate of complications.

A recent review by Velmahos noted that "rates of deep venous thrombosis and pulmonary embolism are widely different even among similar trauma populations," citing an incidence of DVT ranging from 0.5 to 45 percent in comparable populations managed similarly.[5] The review found that 21 of the 31 studies examined found no particular method of prophylaxis to be superior to any other or to no prophylaxis at all. Another analysis of pharmaceutical prophylaxis also concluded that severely injured patients are not protected from PE with the use of prophylactic anticoagulation.[10] It should be noted that the population for this study was comprised entirely of patients in the surgical intensive care unit (ICU) with clinical signs of PE. The observed rate of PE was 37.5 percent.

In a recent multicenter prospective study, Nathens and coworkers[11] showed that delay of initiation of thromboprophylaxis in major trauma was associated with increased incidence of DVT. The inclusion criteria were: patients injured with a blunt mechanism, arrival within 6 hours of injury, blood transfusion within 12 hours of injury, an Abbreviated Injury Scale score of 2 or higher, hypotension (systolic blood pressure <90 mmHg), or acidosis (base deficit $\geq$6) on presentation and admission to the ICU for at least 7 days. The overall incidence of DVT or PE was 11 percent in this significantly injured cohort. If heparin, LMWH, or dalteparin were initiated within 4 days, the risk was 5 percent, but this increased three times to 15 percent if started after 4 days. Certain injury patterns were viewed as having an increased risk of bleeding and therefore led practitioners to delay initiation of prophylaxis. Accordingly, in this study the presence of severe head injury or having received more than 6 units of blood in the first 12 hours corresponded with delayed initiation of DVT prophylaxis. The conclusion is that the tendency of clinicians to reserve initiation of prophylaxis due to risk of increased bleeding may also place injured patients at a greater risk of developing thromboembolic complications, a contradiction that

demonstrates the difficulty in establishing guidelines and protocols.

Current clinical evidence still fails to conclusively support any particular means of prevention or treatment of DVT or PE. The Eastern Association for the Surgery of Trauma (EAST) guidelines published in 2002 were able to provide only the following Level I evidence for prevention of VTE: spinal cord injuries and spinal fractures are at high risk for development of VTE and duplex ultrasound may be used to diagnose symptomatic DVT without the need for venography.[12] No other predictors or methods of diagnosis, prophylaxis, or treatment had sufficient evidence to warrant Level I status (i.e., recommendations based upon prospective, randomized controlled trials, and strong trials focused on prospectively collected data or large retrospective studies with reliable data). The EAST guideline produced several Level II recommendations (i.e., those based on less strong prospectively collected or retrospective studies or insufficient randomized controlled trials) to aid in the clinician's management of patients with VTE, but larger, well-organized studies will still be required to provide definitive evidence and improve clinical outcomes.

CEREBROVASCULAR ACCIDENTS

Cerebrovascular accidents, or strokes, are another possible complication in trauma. In one of the early studies evaluating ischemic neurologic events in trauma, Cogbill and colleagues[13] published a multicenter review identifying 60 symptomatic blunt carotid artery injuries in 49 patients over 6 years. Although an incidence could not be confirmed from this data as it did not include the total number of trauma admissions, the limited number of cases over a 6-year period from 11 trauma institutes reflected the prevailing thought of the time that blunt carotid artery injuries were very rare, possibly present in less than 0.1 percent of injured patients. In the patients with cerebrovascular ischemia, mortality was 43 percent and "good neurological outcome" was achieved in only 45 percent of the surviving patients. This study played a significant role in the recognition of BCVIs as highly morbid, and contributed to the development of screening protocols at several institutions. Protocols based on clinical suspicion, mechanism of injury, and associated injuries then followed, and the previously rarely documented phenomenon became unmasked.

In the following years, several studies reported an increased incidence of carotid, and later vertebral, artery injuries after standardized screening protocols were implemented. Cothren and coworkers[14] performed a 7-year study examining the stroke rate in blunt carotid artery injuries at a single Level I trauma center after implementing a screening protocol based on presenting symptoms, mechanism of injury, and associated injuries. One hundred and fourteen carotid artery injuries were diagnosed by screening angiography (0.9% of 13,280 total blunt trauma admissions). This incidence is consistent with multiple reports of approximately 1 percent cerebrovascular injury in blunt trauma.[15,16] Of the 114 patients, 73 received either antiplatelet agents or anticoagulation, and none developed strokes. The remaining 41 patients were determined to have contraindications to anticoagulation and did not receive heparin or antiplatelet agents. Of these, 19 (46%) developed cerebral ischemia. The conclusion was drawn that early identification through a standardized screening protocol and prompt anticoagulation of blunt carotid artery injuries reduced stroke rate. This paper and those of several other groups suggest that early anticoagulation significantly reduces the stroke rate. However, the retrospective nature of these papers and the low incidence of stroke (though higher than originally thought) limit their applicability and underscore the fact that a large number of patients are required to make definitive statements about this injury.[17,18]

Miller and coworkers[16] reported the outcomes of patients following institution of a screening protocol and compared it with the immediately preceding time period. The screening protocol involved four-vessel cerebral angiography for patients with one or more of the following injuries: cervical spine fracture, neurologic exam not explained by grain imaging, Horner's syndrome, LeFort I or II fractures, skull-base fractures involving the foramen lacerum, or neck soft-tissue injury. The rate of detection of cerebrovascular injury while the protocol was in use was compared with the rate noted in the period prior to the use of a standardized screening system. The authors also secondarily investigated the ability of four-slice computed tomographic angiography and magnetic resonance angiography to diagnose BCVIs compared with standard angiography. This study found that the institution of the screening protocol did not increase the identification of blunt carotid injuries as the incidence in both groups was approximately 0.5 percent. The stroke rate in patients identified with a BCVI was also statistically similar at 33 and 31 percent. The screening protocol did, however, increase the rate of diagnosis of vertebral artery injuries, from 0.4 to 0.7 percent, once the protocol was enacted. There was also a decrease in the stroke rate from vertebral artery injuries from 14 to 0 percent ($p < 0.001$). The overall incidence of BCVI was again approximately 1 percent. Magnetic resonance angiography and computed tomographic angiography both detected BCVIs with a sensitivity of approximately 50 percent. Thus, in 2002, the noninvasive modalities of magnetic resonance angiography and the four-slice computed tomographic angiography were not acceptable screening alternatives to the invasive angiogram.

Further advancements in the field of noninvasive imaging continued to occur and, in 2006, Schneidereit

and colleagues[19] demonstrated an eightfold increase in the rate of diagnosis of BCVIs after implementing an eight-slice computed tomographic angiography-based screening protocol. The incidence of BCVIs increased from 0.17 percent before the screening protocol to 1.4 percent afterward. The delayed stroke rate and mortality also significantly decreased from 67 to 0 percent and 38 to 0 percent, respectively. This study again demonstrated that the efficacy of establishing a screening protocol though the specificity of computed tomographic angiography versus angiography cannot be fully evaluated as only 23 of the 33 patients were evaluated with angiography. Although limited by the relatively small number of patients with vascular neck injuries (n = 33) and the lack of simultaneous use of angiography, this study demonstrated a significant reduction in morbidity and mortality after implementing a screening protocol based on noninvasive methods of detection. As the resolution of computed tomographic angiography continues to improve, 16-slice multidetector computed tomography is being shown to be a highly effective screening tool. Three studies in the past year have demonstrated that 16-slice computed tomographic angiography has comparable sensitivity to angiography and has increased the diagnosis of BCVIs compared with prior screening protocols based on four-slice computed tomographic angiography.[20-22] As noninvasive computed tomographic angiography screening methods continue to improve, they will likely surpass angiography as the standard modality for screening.

In 2002 the role of follow-up arteriography was investigated. This study reviewed 171 patients with a total of 157 carotid artery injuries and 97 vertebral artery injuries.[15] The stroke rate was 23 percent for those with carotid injuries and 20 percent for those with vertebral injuries, with an overall mortality of 14 and 10 percent, respectively. Repeat arteriography was performed between postinjury Days 7 and 10 for 73 percent of the carotid injuries and 62 percent of the vertebral injuries. Fifty-seven percent of the Grade I lesions for either carotid or vertebral arteries demonstrated a healed vessel at repeat imaging, whereas 8 percent progressed to pseudoaneurysm formation. Of the Grade II injuries imaged, 8 percent healed and 43 percent had advanced to pseudoaneurysm formation. Upon diagnosis of progression of the injuries to pseudoaneurysm, the lesions were either stented or embolized. The authors determined that repeat imaging led to a change in management in 51 percent of the patients with Grade I or II injuries; however, this change was not observed for the higher-grade injuries. Side effects and complications were reported in this analysis, and 4 of the 171 patients developed strokes attributable to the procedures. Additional complications included one transient ischemic attack, three puncture site hematomas, and a subclavian artery dissection.

In addition to blunt trauma as a mechanism for carotid artery injury and subsequent stroke, cases of penetrating internal carotid artery injury with delayed onset of neurologic symptoms have also been reported, although few large series have been published.[23] Kuehne and colleagues[24] reported 61 cases of penetrating internal carotid injuries from 1975 to 1995, comparing the first 10 years, during which the management was at the discretion of the surgeon, with the following 10 years in which a clinical treatment algorithm had been implemented. The protocol consisted of diagnostic angiography for stable patients with suspected internal carotid injuries, followed by reconstruction of surgically accessible injuries. Neurologically stable patients with complete internal carotid artery occlusion were treated nonoperatively with anticoagulation, while nonocclusive injuries were followed with serial duplex ultrasonography or angiography. The study focused on neurologic status at admission and discharge. From 1975 to 1985, 12 of the 36 patients (33%) presented with a neurologic deficit, and at discharge 17 percent had improved, 66 percent were unchanged, and 17 percent had worsened. Following institution of the standardized diagnostic and treatment guidelines, 6 of the 25 patients (24%) presented with a deficit, with 12 percent improving, 88 percent remaining unchanged, and none worsening. Overall, 30 percent of the patients admitted with penetrating trauma to the internal carotid artery demonstrated neurologic deficit.

While BCVIs appear to occur in approximately 1 percent of all blunt trauma admissions and subsequent neurologic deficit from these injuries approaches an incidence of 20 to 30 percent, the overall rate of stroke in the total trauma population has not been widely investigated. Mechanisms for neurologic ischemia and damage other than carotid or vertebral artery occlusion exist, such as intracranial hemorrhage following hypertension and ischemia due to hypoperfusion during shock. Cerebrovascular injury is only one mechanism, and a true incidence in trauma is yet to be discerned.

In contrast to the plethora of publications regarding DVT, PE, and neurologic deficits in blunt cerebrovascular trauma, there is very little published to date regarding the incidence of two other thromboembolic phenomena: MI and mesenteric thrombosis.

MYOCARDIAL INFARCTION

Heart disease is the leading cause of death in the United States.[25] Factors such as escalating age of the population, increasing obesity, and improved survival from initial injuries with developed trauma systems may lead to increased incidence of posttraumatic MI. The true overall incidence of MI after injury is not known. Postinjury MI may be due to direct trauma to the heart, disruption of the lumen of a coronary vessel, or as a cumulative result of the

physiologic stresses of trauma, such as hypoxia, hypotension, or catecholamine surge.

Blunt cardiac trauma is one of the more commonly reported mechanisms of injury in trauma patients that develop posttraumatic MI, although no studies have categorized the incidence over a period of time. Guldner and coworkers[26] reviewed the literature and found 63 cases of coronary artery occlusion following blunt chest trauma. The review focused on young patients (age 15-40 years) with no preexisting risk factors for MI who developed MI following blunt chest trauma. The diagnosis was confirmed by angiography or at autopsy. In an effort to ensure that the cause of the MI was from the blunt chest trauma, patients were eliminated if there was an asymptomatic period between the time of injury and that of diagnosis of the MI, although the specific time interval used for exclusion was not discussed. While this study showed multiple cases of MI following a common mechanism, it did not focus on the overall incidence of MI and eliminated those MIs that occur with a delayed presentation and the elderly population in whom MI is most likely.

Ismailov and colleagues[27] investigated the types of injuries associated with myocardial infarcts. A review of all hospital discharges from 19 participating states for a single year yielded more than 1 million cases with ICD-9-CM codes indicating blunt trauma (codes 800-959). The patients were then categorized into subsets by anatomic location of injury, including thoracic trauma, abdominal and pelvic trauma, spine and back trauma, and blunt cardiac trauma by subsets of the ICD-9-CM codes. Of these, 32,616 (3.10%) also included the code for acute MI. Multivariate logistic regression identified blunt cardiac injury as well as abdominal or pelvic trauma as significant risk factors for developing MI. This study is limited by its retrospective nature and an inability to confirm the diagnosis of MI other than by discharge coding; thus the temporal relationship of the MI and injury cannot be established. The most common mechanism of injury in patients with MI was a fall. Did the fall occur as a result of the MI or did the MI result from the trauma? Falls, increasing age, and MIs are likely related. While the patient population was very large, it included only blunt injuries and excluded burns and penetrating injuries. As such, not all of the trauma admissions were incorporated into the study, and it again fails to represent the total trauma population. For example, skull fractures, intracranial injuries, and extremity trauma were excluded. The exclusion of patients with intracranial injuries and extremity injuries eliminates a patient population previously demonstrated to be at increased risk for other types of thromboembolic complications following trauma, such as DVT and PE, and potentially at higher risk for MI.

A report of MI following injury over a 10-year period at a single Level I trauma center was published in 2000.[28] Patients were included if they were coded as having an MI during the admission and had at least two of the following documented: classic symptoms of MI, elevation of cardiac isoenzymes, or electrocardiogram changes consistent with MI. To eliminate those patients presenting with an immediate MI, the exclusion criteria included immediate rise in cardiac enzymes, although, again, the specific time interval was not noted. In contrast to Guldner's analysis in which patients with an asymptomatic period between injury and diagnosis were excluded, this paper eliminated patients who had an immediate rise in serum markers in an effort to avoid inclusion of patients who had the MI prior to the injury, thus including only those patients who developed the condition as a complication of their injury. Nineteen patients were identified as possibly sustaining MI, but 14 were excluded. Five were eliminated because it could not be determined if the MI preceded or followed the trauma, one preceded the trauma, and eight did not meet the inclusion criteria for MI. A total of five verified MIs were noted in the 11,866 patients reviewed (0.04%). Of these, the causes of injury were fall, stab, burn, and two motor vehicle collisions. If all 19 cases were presumed to have a posttraumatic MI, the resulting incidence would be 0.16 percent. Although the incidence of MI in this study is low, there have not been subsequent large studies confirming this finding. The authors reiterated their belief "that this report almost certainly underestimates the true frequency of post-injury MI."

Dodge and colleagues[29] demonstrated a case of MI in a 10-year review of gunshot wounds. This paper reported 122 cases of gunshot wounds over 10 years at a rural Level II trauma center. Of the 25 deaths, 1 was the result of an acute MI. Again, while this does not report the incidence of nonfatal MI, it demonstrates MI associated with penetrating trauma.

Though commonly excluded from the trauma literature, patients with burns frequently demonstrate a hyperdynamic state and warrant consideration in the evaluation of MI. Goff and coworkers[30] demonstrated an increased incidence of MI and cardiac disease in burn patients versus those without burns. Eight percent of the burn admissions experienced an in-hospital MI and mortality after the MI was 3.5 to 4 times higher in patients with burns compared with nonburned patients. While most severely burned patients are treated at specialty facilities, it is important to consider the increased risk in this population.

MESENTERIC VENOUS AND ARTERIAL THROMBOSIS

Another uncommon thromboembolic complication following injury is mesenteric thrombosis. Case reports are rare and no studies have reported an overall incidence in trauma. In 1952 McCune and colleagues[31] presented four cases of mesenteric thrombosis following blunt

abdominal trauma which occurred from 1936 to 1950. Cole and colleagues[32] reported a case of mesenteric thrombosis in a patient with penetrating cardiac trauma. In both reports the prime contributing mechanism was suspected to be a low-flow state through the mesenteric vessels. The Cole article specifically asserts that surviving an injury in which persistent hypotension occurred may predispose the patient to developing mesenteric venous thrombosis. Additional causes of vascular occlusion noted in the literature are thrombus formation at the site of an arterial anastamosis or presence of a preexisting hypercoagulable disorder such as antiphospholipid syndrome.[33,34] The early studies made the diagnosis of mesenteric thrombosis at laparotomy, while more recently the condition has been confirmed by computed tomography. Recently, in a randomized, placebo-controlled, double blind clinical trial evaluating the efficacy and safety of recombinant activated factor VIIa in trauma patients, a member of the control group was noted to have developed a mesenteric vein thrombus while none occurred in the treatment group for an incidence of 0.3 percent (1/301).[35]

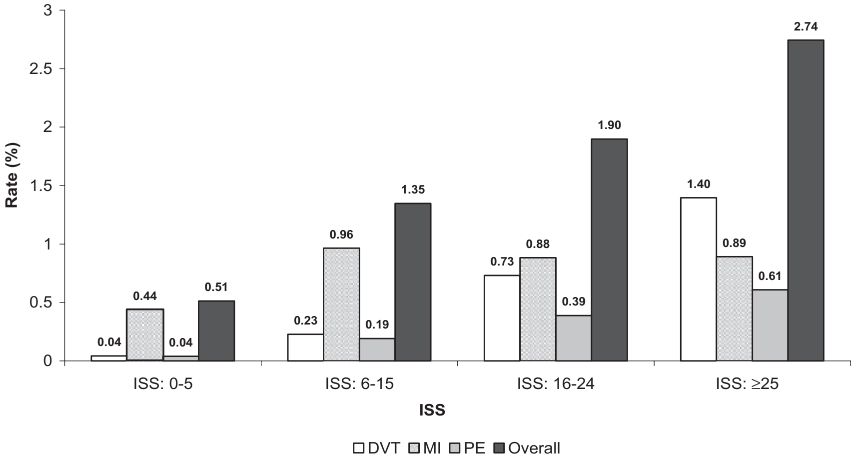

Fig. 1. Increasing rate of thrombotic complications for DVT, MI, and PE, by ISS based on data from the NTDB, http://www.facs.org/trauma/ntdb.html; n = 952,242; average ISS for the entire population = 9.6.

TABLE 1. Incidence of thromboembolic complications cited in reviewed studies and reported in the NTDB, http://www.facs.org/trauma/ntdb.html

	Reviewed literature	NTDB n = 952,242; ISS = 9.6
DVT	0.2-58%	0.3%
PE	0.1-37.5%	0.2%
MI	0.04-3.1%	0.7%
Cerebrovascular accident	0.14-33%	—
Mesenteric thrombosis	Case reports	—

NATIONAL TRAUMA DATA BANK

The NTDB version 5.0 was queried to determine the incidence of the five thromboembolic complications discussed in this report. Only three of the five complications were available for analysis: DVT, PE, and MI (Fig. 1). Stroke and mesenteric thrombosis are not listed as reportable complications in the NTDB. The reported rates in both the reviewed literature and the NTDB are shown in Table 1. In an attempt to correlate the presumed increase in thrombotic complications with increasing injury, the data in Table 1 were grouped according to increasing ISS (Table 1). The individual and total thrombotic complications increased by at least a factor of 5 when ISS increased from 5 to 25.

CONCLUSIONS

Thromboembolic events are known complications of trauma. The incidence of the more common thromboembolic complications of DVT, PE, and cerebrovascular accidents continues to be elucidated, while those of more rare complications, such as MI and mesenteric thrombosis, exist primarily as case reports. There is a staggering range in the reported incidence of thrombotic complications. Disparities in populations studied and standardization of screening means of diagnosis, prophylaxis, and treatment contribute to the uncertainty in this area. Questions remain as to which specific patient populations require prophylaxis, which agent or agents, if any, should be used, and when they should be started. It is recognized that thromboembolic events occur at a greater rate in more severely injured patients. As concepts such as damage control laparotomy and changes in initial resuscitation continue to gain favor, patients are more likely to survive the acute phase of their injury. Adding to the confusion are the increased uses of several prohemostatic and antifibrinolytic agents. Along with advances in critical care, patients are now more likely to survive injuries that in the past would have been lethal. The paradox is that in improving eventual outcomes, more severely injured patients will survive and therefore increase the possibility of developing thromboembolic complications. As such, many of the events can be thought of as complications of survivorship. Lastly, extreme caution must be used when attributing thrombotic causality, especially in small uncontrolled case series of seriously injured patients.[36,37] Because of the relative rarity of these events and

documented increased incidence with increasing injury severity, guidelines based on large, well-designed, multicenter, and controlled studies will be required to answer many of these questions.

DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

1. Mccartney J. Pulmonary embolism following trauma. Surg Gynecol Obstet 1935;61:369-79.
2. Franco RF, Reitsma PH. Genetic risk factors of venous thrombosis. Hum Genet 2001;109:369-84.
3. Knudson MM, Ikossi DG. Venous thromboembolism after trauma. Curr Opin Crit Care 2004;10:539-48.
4. Rogers F, Rebuck JA, Sing RF. Venous thromboembolism in trauma: an update for the intensive care unit practitioner. J Intensive Care Med 2007;22:26-37.
5. Velmahos GC. The current status of thromboprophylaxis after trauma: a story of confusion and uncertainty. Am Surg 2006;72:757-63.
6. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. N Engl J Med 1994;331:1601-6.
7. Knudson MM, Ikossi DG, Khaw L, Morabito D, Speetzen LS. Thromboembolism after trauma: an analysis of 1602 episodes from the American College of Surgeons National Trauma Data Bank. Ann Surg 2004;240:490-6; discussion 496-8.
8. Knudson MM, Morabito D, Paiement GD, Shackleford S. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. J Trauma 1996; 41:446-59.
9. Stawicki SP, Grossman MD, Cipolla J, Hoff WS, Hoey BA, Wainwright G, Reed JF 3rd. Deep venous thrombosis and pulmonary embolism in trauma patients: an overstatement of the problem? Am Surg 2005;71:387-91.
10. Velmahos GC, Toutouzas KG, Brown C, Vassiliu P, Gkiokas G, Rhee P. Thromboprophylaxis does not protect severely injured patients against pulmonary embolism. Am Surg 2004;70:893-6.
11. Nathens AB, McMurray MK, Cuschieri J, Durr EA, Moore EE, Bankey PE, Freeman B, Harbrecht BG, Johnson JL, Minei JP, McKinley BA, Moore FA, Shapiro MB, West MA, Tompkins RG, Maier RV. The practice of venous thromboembolism prophylaxis in the major trauma patient. J Trauma 2007;62:557-62; discussion 562-3.
12. Rogers FB, Cipolle MD, Velmahos G, Rozycki G, Luchette FA. Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST practice management guidelines work group. J Trauma 2002;53:142-64.
13. Cogbill TH, Moore EE, Meissner M, Fischer RP, Hoyt DB, Morris JA, Shackford SR, Wallace JR, Ross SE, Ochsner MG. The spectrum of blunt injury to the carotid artery: a multicenter perspective. J Trauma 1994;37:473-9.
14. Cothren CC, Moore EE, Biffl WL, Ciesla DJ, Ray CE Jr, Johnson JL, Moore JB, Burch JM. Anticoagulation is the gold standard therapy for blunt carotid injuries to reduce stroke rate. Arch Surg 2004;139:540-5; discussion 545-6.
15. Biffl WL, Ray CE Jr, Moore EE, Franciose RJ, Aly S, Heyrosa MG, Johnson JL, Burch JM. Treatment-related outcomes from blunt cerebrovascular injuries: importance of routine follow-up arteriography. Ann Surg 2002;235:699-706; discussion 706-7.
16. Miller PR, Fabian TC, Croce MA, Cagiannos C, Williams JS, Vang M, Qaisi WG, Felker RE, Timmons SD. Prospective screening for blunt cerebrovascular injuries: analysis of diagnostic modalities and outcomes. Ann Surg 2002;236: 386-93; discussion 393-5.
17. Biffl WL, Moore EE, Ryu RK, Offner PJ, Novak Z, Coldwell DM, Franciose RJ, Burch JM. The unrecognized epidemic of blunt carotid arterial injuries: early diagnosis improves neurologic outcome. Ann Surg 1998;228:462-70.
18. Fabian TC, Patton JH Jr, Croce MA, Minard G, Kudsk KA, Pritchard FE. Blunt carotid injury. Importance of early diagnosis and anticoagulant therapy. Ann Surg 1996;223: 513-22; discussion 522-5.
19. Schneidereit NP, Simons R, Nicolaou S, Graeb D, Brown DR, Kirkpatrick A, Redekop G, McKevitt EC, Neyestani A. Utility of screening for blunt vascular neck injuries with computed tomographic angiography. J Trauma 2006;60: 209-15; discussion 215-6.
20. Berne JD, Reuland KS, Villarreal DH, McGovern TM, Rowe SA, Norwood SH. Sixteen-slice multi-detector computed tomographic angiography improves the accuracy of screening for blunt cerebrovascular injury. J Trauma 2006; 60:1204-9; discussion 1209-10.
21. Biffl WL, Egglin T, Benedetto B, Gibbs F, Cioffi WG. Sixteen-slice computed tomographic angiography is a reliable noninvasive screening test for clinically significant blunt cerebrovascular injuries. J Trauma 2006;60:745-51; discussion 51-2.
22. Utter GH, Hollingworth W, Hallam DK, Jarvik JG, Jurkovich GJ. Sixteen-slice CT angiography in patients with suspected blunt carotid and vertebral artery injuries. J Am Coll Surg 2006;203:838-48.
23. Agrawal A, Kumar A, Tiwari A, Sinha A, Patel A. Low velocity traumatic dissection of the internal carotid artery presenting as a stroke after a slash injury. Singapore Med J 2007;48:e127-9.
24. Kuehne JP, Weaver FA, Papanicolaou G, Yellin AE. Penetrating trauma of the internal carotid artery. Arch Surg 1996; 131:942-7; discussion 947-8.
25. Centers for Disease Control and Prevention. Deaths: leading causes for 2003. Natl Vital Stat Rep 2007;55:1-93.

26. Guldner GT, Schilling TD. Coronary artery occlusion following blunt chest trauma: a case report and review of the literature. Can J Emerg Med 2005;7:118-23.
27. Ismailov RM, Ness RB, Weiss HB, Lawrence BA, Miller TR. Trauma associated with acute myocardial infarction in a multi-state hospitalized population. Int J Cardiol 2005;105:141-6.
28. Moosikasuwan JB, Thomas JM, Buchman TG. Myocardial infarction as a complication of injury. J Am Coll Surg 2000;190:665-70.
29. Dodge GG, Cogbill TH, Miller GJ, Landercasper J, Strutt PJ. Gunshot wounds: 10-year experience of a rural, referral trauma center. Am Surg 1994;60:401-4.
30. Goff DR, Purdue GF, Hunt JL, Cochran RP. Cardiac disease and the patient with burns. J Burn Care Rehabil 1990;11:305-7.
31. McCune WS, Keshishian JM, Blades BB. Mesenteric thrombosis following blunt abdominal trauma. Ann Surg 1952;135:606-14.
32. Cole FH Jr, Richardson RL. Mesenteric thrombosis after penetrating cardiac trauma. South Med J 1976;69:1517-8.
33. Fried M, Van Ganse W, Van Avermaet S. Mesenteric vein thrombosis triggered by blunt abdominal trauma in a patient with the primary antiphospholipid syndrome. Eur J Gastroenterol Hepatol 2002;14:697-700.
34. Lucas AE, Richardson JD, Flint LM, Polk HC Jr. Traumatic injury of the proximal superior mesenteric artery. Ann Surg 1981;193:30-4.
35. Boffard KD, Riou B, Warren B, Choong PI, Rizoli S, Rossaint R, Axelsen M, Kluger Y. Recombinant factor VIIa as adjunctive therapy for bleeding control in severely injured trauma patients: two parallel randomized, placebo-controlled, double-blind clinical trials. J Trauma 2005;59:8-15; discussion 15-8.
36. O'Connell KA, Wood JJ, Wise RP, Lozier JN, Braun MM. Thromboembolic adverse events after use of recombinant human coagulation factor VIIa. JAMA 2006;295:293-8.
37. Thomas GO, Dutton RP, Hemlock B, Stein DM, Hyder M, Shere-Wolfe R, Hess JR, Scalea TM. Thromboembolic complications associated with factor VIIa administration. J Trauma 2007;62:564-9.